INTRODUCTION

Asthma is a chronic inflammatory disease of the airways that has created a significant public health burden. In the United States, more than 11 million people reported having an asthma attack in the year 2000, and more than 5 percent of all children younger than age 18 reported having asthma attacks. In 1999, asthma was responsible for 2 million emergency department visits, 478,000 hospitalizations with asthma as a primary diagnosis, and 4,426 deaths. The rates of hospitalization have remained the same or lower since 1980 for all age groups, except children younger than age 15. Mortality rates have declined overall since 1995, but a disparity among ethnic groups remains: Asthma mortality is nearly 3 times higher in black males than in white males and 2.5 times higher in black females than in white females (Centers for Disease Control and Prevention).

Scientific advances over the last 15 years have led to a greater understanding of the mechanisms of asthma and the development of therapeutic approaches that can reduce morbidity and improve the quality of life among persons with asthma. To help health care professionals bridge the gap between current knowledge and practice, the National Heart, Lung, and Blood Institute's (NHLBI's) National Asthma Education and Prevention Program (NAEPP) has convened expert panels to prepare clinical practice guidelines for the diagnosis and management of asthma. The NAEPP Coordinating Committee, under the leadership of Claude Lenfant, M.D., director of the NHLBI, convened the first Expert Panel in 1989. The Panel was charged with developing a report that would provide a general approach to diagnosing and managing asthma based on current science. The NAEPP *Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma* (NAEPP 1991) was published in 1991. Recommendations for the treatment of asthma were organized around the following four components of effective asthma management:

- Use of objective measures of lung function to assess the severity of asthma and to monitor the course of therapy
- Environmental control measures to avoid or eliminate factors that contribute to asthma severity
- Comprehensive pharmacologic therapy for long-term management designed to reverse and prevent the airway inflammation characteristic of asthma, as well as pharmacologic therapy to manage asthma exacerbations
- Patient education that fosters a partnership among the patient, his or her family, and clinicians.

The NAEPP convened a second Expert Panel in 1995 to review the entire 1991 report and update it, if necessary, based on review of the literature published since 1991 and on clinical experience with implementation of the report's recommendations for clinical practice. The NAEPP *Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma* (EPR-2) was published in 1997.

The NAEPP recognizes that the value of clinical practice guidelines lies in their presentation of recommendations based on the best and most current evidence available. However, high-quality research on all areas of asthma management is not available, and scientific examination and discovery often is focused on only a few areas at any given time. The NAEPP concluded that an efficient approach to updating the clinical practice guidelines would be to identify selected questions that warrant intensive review and possible update, based on either the level of research activity reflected in the published literature or the level of concern or controversy in clinical practice. Position statements on these topics would be published as NAEPP *Expert Panel Report Updates,* and would be incorporated into the Web-based version of EPR-2. Thus, the NAEPP *Expert Panel Report* is a dynamic document that will be updated continuously with position statements on topics of interest to the community of patients, clinicians, and organizations dedicated to improving asthma care.

The NAEPP charged its Science Base Committee with the responsibility for monitoring the scientific literature, identifying topics for review, determining the need for changes in the EPR-2, and preparing appropriate updates. The Science Base Committee is a multidisciplinary group of clinicians and scientists with expertise in asthma management. The group includes health professionals in the areas of general medicine, family practice, pediatrics, emergency and critical care, allergy, pulmonary medicine, pharmacy, and health education. The Science Base Committee reports to the NAEPP Coordinating Committee, which comprises representatives from 40 professional societies, voluntary organizations, and Federal agencies.

This report, the NAEPP *Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma Update on Selected Topics—2002,* presents recommendations for the management of asthma that will help clinicians and patients make appropriate decisions about asthma care on the following topics:

- Medications
  - Long-term management of asthma in children:
    - ♦ Effectiveness of inhaled corticosteroids for children with mild or moderate persistent asthma compared with other medications
    - ♦ Safety of long-term use of inhaled corticosteroids
  - Combination Therapy: The addition of other long-term-control medications to inhaled corticosteroids
  - The effect of antibiotics on acute asthma exacerbations

- Monitoring
  - Written asthma management plans compared to medical management alone
  - Peak flow-based compared to symptom-based written action plans
- Prevention
  - Effects of early treatment on the progression of asthma.

The appendixes to this report contain updated stepwise and dosage charts and a list of abbreviations and acronyms.

This report revises the EPR-2 Stepwise Approach for Managing Asthma to incorporate findings from the review of the scientific evidence. These guidelines are intended to inform, not replace, clinical judgment. Of course, the clinician and patient need to develop individual treatment plans that are tailored to the specific needs and circumstances of the patient. This report is not an official regulatory document of any Government agency.

Methods Used To Develop This Report

The NAEPP Science Base Committee met in April 1999 to identify priority areas for review and possible update of recommendations in EPR-2. The Committee used a modified Delphi technique to rank all major EPR-2 clinical recommendations according to whether major new studies had been published in that area or the area was of considerable clinical interest but lacking in consistent evidence at the time EPR-2 was developed. At the same time, the Agency for Healthcare Research and Quality (AHRQ), through its own routine process of soliciting questions from the medical community for the development of evidence reports, received questions on asthma from the American Academy of Pediatrics and the American Academy of Family Physicians. Several of the topics were comparable to those identified by NAEPP Science Base Committee, so the NHLBI worked with the AHRQ to develop a contract with an AHRQ Evidence-Based Practice Center. An AHRQ contract was awarded to the Blue Cross Blue Shield Association Technology Evaluation Center to conduct a systematic review of the evidence (SRE) on the topics listed earlier.

In August 1999, the AHRQ Evidence-Based Practice Center began to perform comprehensive review of the literature on each of the selected topics; to prepare evidence tables depicting study design, research variables, and reported outcomes; and to summarize the literature findings in a narrative report. This report, however, was not intended to make judgments about the implications of the findings for clinical practice. The Evidence-Based Practice Center's methods for conducting the SRE are described in detail elsewhere (Blue Cross and Blue Shield Association Technology Evaluation Center) and are summarized here.

- The Evidence-Based Practice Center formed a Technical Advisory Group composed of asthma specialists and primary care physicians, including several members of the NAEPP Science Base Committee. The literature search included full-length reports published in peer-reviewed medical journals and articles in English or published in foreign languages with English abstracts. Studies that did not include control groups in the research design were excluded from review (except for those that dealt with the topic of adverse effects of inhaled corticosteroids), and most of the included trials were randomized. Specific criteria that defined patient populations of interest, outcomes of interest, types of interventions, and study design were established for each topic. A comprehensive literature search was performed using key text words and MeSH terms (Medical Subject Heading) to identify all relevant controlled clinical trials. (Key words included, for example, all long-term-control asthma medications, antibiotics in asthma, peak expiratory flow rate meter, action plan, and self-care monitoring.) Both the MEDLINE and EMBASE databases were searched for all articles published from 1980 through August 2000. In addition, the search included potentially relevant studies published before 1980 but referenced in the post-1980 literature.
- The search retrieved 4,235 English and 343 non-English language references. One member of the Evidence-Based Practice Center's study team reviewed abstracts; a second team member reviewed any excluded abstracts. On the basis of this abstract review, 668 full-length journal articles were retrieved and rated independently by two study team members against study selection criteria. Eighty-seven articles met the study selection criteria to be included in the SRE. Data from these 87 articles were abstracted for evidence tables by two reviewers and were recorded in an electronic database. Data elements included categories such as study design and methods, patient characteristics, lung function outcomes, symptom outcomes, medication outcomes, utilization outcomes, and adverse events.
- A quality assessment of the studies was performed to enable sensitivity analysis comparing the results and conclusions reached from all included studies with the results and conclusions of a subgroup of higher quality studies. Quality was assessed on three domains: concealment of treatment allocation during randomization, double-blinding, and handling of withdrawals and exclusions. Quality also was assessed on domains deemed pertinent to asthma research, such as establishing reversibility of airway obstruction, controlling for other medication use, reporting compliance, addressing seasonality, and a priori reporting of power calculations.
- A meta-analysis was performed to assess the benefits of adding long-acting inhaled $beta_2$ agonist medication to inhaled corticosteroids as treatment of moderate persistent asthma.

In February 2001, the Evidence-Based Practice Center submitted a draft report of the SRE to the AHRQ. The NAEPP Science Base Committee, serving as an Expert Panel, met in March to review the Evidence-Based Practice Center's report and to interpret the implications for

clinical practice and the recommendations included in EPR-2. The Expert Panel reached consensus on whether the evidence supported the recommendations made in EPR-2 or indicated a need for revision. The Expert Panel then assigned writing committees to develop position statements on each of the topics. Each Panel member was assigned to one of the writing committees. The Expert Panel noted that, for some topics, significant studies had been published in the 7-month period between the Evidence-Based Practice Center's search of the literature and the submission of its report. The Expert Panel agreed that the writing committees would include their own review of additional literature published since August 2000 and use MEDLINE searches as appropriate. The distinction between the two literature reviews is noted in the position statements by separating discussion of the Evidence-Based Practice Center's *Systematic Review of the Evidence* (SRE) and the Expert Panel's *Additional Literature or Information.* Further, the source and level of the evidence used to justify Panel recommendations for sustaining or revising EPR-2 are noted in parentheses following the recommendation. (That is, the level of evidence is categorized A, B, C, or D according to the description below. If the source of the evidence is from the SRE, the category is preceded by the notation "SRE"; if the source is the Expert Panel's additional literature, there is no prefix.) The system used to describe the level of evidence is as follows (Jadad et al. 2000):

- **Evidence Category A: Randomized controlled trials (RCTs), rich body of data.** Evidence is from end points of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
- **Evidence Category B: RCTs, limited body of data.** Evidence is from end points of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
- **Evidence Category C: Nonrandomized trials and observational studies.** Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
- **Evidence Category D: Panel Consensus Judgment.** This category is used only in cases where the provision of some guidance was deemed valuable, but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel consensus is based on clinical experience or knowledge that does not meet the criteria for categories A through C.

As the Expert Panel members reviewed the scientific evidence and considered revisions to EPR-2, they identified areas that require further investigation to either fill important gaps found in the data or to pursue promising areas of research revealed by study findings. Each position statement includes recommendations for further research.

The Expert Panel prepared draft position statements in its respective writing committees during summer and fall 2001, and the drafts were edited during the winter. A series of drafts were discussed in three telephone conference calls (June 2001, October 2001, and February 2002) among the full Panel membership. Final agreement on each position statement was reached during these calls, including the specific recommendations within the position statements to either retain or revise EPR-2. A vote confirmed the unanimous agreement of the Panel. In March 2002, a draft was mailed to the NAEPP Coordinating Committee members for their review, comment, and approval. In April 2002, the Expert Panel reviewed the Coordinating Committee's suggested edits by e-mail and by telephone conference call and incorporated suggestions that were within the scope of the Coordinating Committee's approval. Expert Panel members' agreement on the final text was unanimous. The NAEPP *Expert Panel Report Update—2002* was released in June 2002.

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In summary, the NAEPP *Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Questions—2002* represents the NAEPP's ongoing effort to keep recommendations for clinical practice up to date and based on systematic review and consideration of the best available scientific evidence, as well as on the collective expertise of the Expert Panel and Coordinating Committee members in asthma management. The NAEPP hopes that this report will assist clinicians and patients as they work together to achieve asthma control.

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